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INTERACTION INITIATIVES BETWEEN REGULATORY, HEALTH TECHNOLOGY ASSESSMENT AND COVERAGE BODIES, AND INDUSTRY

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There has been an increased focus on the relationship between health technology assessment (HTA) and regulatory assessments and how regulatory, HTA and coverage bodies, and industry can work better together to improve efficiency and alignment of processes. There is increasingly agreement across sectors that improved communication and coordination could contribute to facilitating timely patient access to effective, affordable treatments that offer value to the health system. Discussions on aspects of this relationship are being held in different forums and various forms of coordination and collaboration are being developed or piloted within several jurisdictions. It is therefore both timely and of value to stakeholders to describe and reflect on current initiatives intended to improve interactions between regulatory, HTA and coverage bodies, and industry. Drawing on 2011 meetings of the HTAi Policy Forum and the Center for Innovation in Regulatory Science (CIRS), this study aims to describe and compare initiatives, and point to success factors and challenges that are likely to inform future work and collaboration.

Keywords: Decision making, Health, Health policy, Insurance coverage, Regulatory approval, Reimbursement, health insurance, Technology assessment, Biomedical

Both regulatory and coverage body representatives are beginning to call for greater alignment between their respective systems, and recently there has been an increased focus on ways in which regulatory, health technology assessment (HTA), and coverage bodies can work better together within their remits (2;5;6;20;21). Interactions in this field have primarily concerned the regulatory approval and coverage of pharmaceuticals, although many issues are also relevant to diagnostics and medical devices.

The primary reasons for increased interest in improving interaction among regulatory, HTA, and coverage bodies include: (i) patients, the public, and policy makers have a high level of awareness of discrepancies between positive market authorization decisions of regulatory bodies and negative coverage decisions, and are therefore questioning the degree of consistency and alignment that exists between these; (ii) coverage bodies are cognizant that most evidence generated by manufacturers is tailored to meet regulatory requirements, and does not fully satisfy the evidentiary requirements of HTA undertaken to support coverage decisions (e.g., for data on effectiveness rather than efficacy, for quality of life measurement, for comparative studies, and for cost data); (iii) the use of conditional and progressive coverage decisions has contributed to interest among regulators, HTA, and coverage bodies in opportunities to align post marketing data collection, and (iv) there is a prevalent view that better communication, and coordination when possible, may improve the efficiency of review processes, and possibly reduce unnecessary differences in evidentiary requirements (recognizing that these will nonetheless continue to differ in some areas) (5;20).

Efforts to enhance coordination among regulatory, HTA, and coverage bodies place demands on scarce resources; thus, it is incumbent upon those involved to share lessons learned. This study describes and reflects on the different initiatives intended to improve the interaction between regulatory, HTA and coverage bodies, and industry, points to key success factors, and suggests ways in which these findings may inform future work and collaboration.

Regulatory Authorities

Countries regulate the entry of therapeutic technologies onto their markets to protect and promote the health of their populations. Key roles of regulatory authorities are the assessment of quality, safety, and efficacy of pharmaceuticals, and safety and technical performance of devices. Such regulation is normally conducted at the national level within a government agency reporting to the Ministry of Health. An exception to this is the European Medicines Agency (EMA), which is a centralized agency of the European Union (EU) (8). Market authorization of products evaluated by EMA applies to all EU member states.

For pharmaceuticals, regulatory assessment is traditionally done on the basis of confirmatory studies, typically using

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placebo-controlled trials and using data provided by manufacturers. Usually only information about approved products is made publically available, and the extent of transparency varies; however, industry is increasingly registering all trials in international databases, and may be challenged regarding the outcomes of their studies. In the past 30 years, interaction between regulatory bodies and industry has increased, and today many regulators engage with industry during product development by providing scientific advice on individual products.

Coverage Bodies

The term "coverage body" is used here to refer to private or public organizations involved in deciding whether or not to include or provide reimbursement for a new technology in a particular healthcare system. These organizations may be national, regional or local, and are responsible for populations from thousands to hundreds of millions.

The key role of most coverage bodies is to consider the value of a technology for the patients for whom they are responsible, and the impact of its inclusion on the healthcare budget. Therefore, therapeutic value and affordability are generally key issues underpinning coverage decisions. Due to uncertainties surrounding the evidence base for new technologies, price and/or access is often determined through negotiation between the manufacturer and coverage body. Hence, as access to medicines is a political as well as economic issue, coverage bodies are increasingly turning to HTA to reduce such uncertainty, and provide a more evidentiary approach to their decision-making process.

HTA for Coverage Decisions

HTA is used to support decisions about health technologies in many national, regional, and local healthcare systems (18). HTA seeks to assess clinical- and sometimes cost-effectiveness along with wider implications of a health technology in comparison to the usual standard of care in a particular healthcare setting. HTA, therefore, requires evidence on clinical outcomes that are meaningful to patients and healthcare systems, as well as costs and consequences of using the technology. This evidence is often not available from confirmatory trials and other pre-marketing studies, therefore, extensive modeling and extrapolation of data from other sources such as patient registries, and observational studies may need to be undertaken.

Except for newly approved medicines where evidence is supplied by the manufacturer, HTA is usually based on publicly available studies and any further evidence provided by manufacturers. Most HTAs performed by public bodies are published, and existing HTAs are often drawn upon by other HTA and/or coverage bodies when considering the same technology. Several HTA agencies now offer scientific advice to industry (i.e., on study design, outcomes, comparators, etc.), but this is a recent development and rather limited compared with regulatory-industry interactions.

SOURCES OF INFORMATION AND DEFINITIONS

Information on initiatives considered in this study comes primarily from presentations and discussions held at the Health Technology Assessment international (HTAi) Policy Forum Meeting January–February 2011 (19;20) and the Centre for Innovation in Regulatory Science (CIRS) Workshop held in March–April 2011 (4;5) (Supplementary Material, which can be viewed online at www.journals.cambridge.org/thc2012041).

This study refers to definitions of regulatory approval, HTA and coverage used in the policy brief issued from the HTAi Policy Forum Meeting 2011 (20), and to the definitions of efficacy, relative efficacy, effectiveness, and relative effectiveness (of a product or health intervention) developed by the European Union High Level Pharmaceutical Forum (11).

DESCRIPTION OF INTERACTION INITIATIVES

An overview of interaction initiatives between regulators, HTA and coverage bodies intended to improve interaction is provided in Table 1, which includes information about the type of interaction, region(s), and stakeholders involved with their homepage indicated. Thus, in this section only documentation on the specific agreements made publicly available are referenced. Whereas some countries provide the option for pre-authorization consultations and/or reviews, others are in initial phases of establishing an offer.

NATIONAL INTERACTIONS

Australia

In Australia, the Therapeutic Goods Administration (TGA) is responsible for evaluating quality, safety and efficacy of drugs and medical devices with the delegate of the Minister of Health making the final decision regarding registration. The Pharmaceutical Benefits Advisory Committee (PBAC) makes the recommendation to the Minister on whether a drug should be listed under the national Pharmaceutical Benefits Scheme (PBS), and the Prostheses and Devices Committee (PDC) makes reimbursement recommendations about surgically implanted devices and tissues.

Shared Scientific Advice (TGA and PBS). Industry may seek advice from both TGA and PBS before submission of their dossiers for review, and also on the design of Phase III trials (5;19). Advice on dossiers typically occurs in bipartite meetings between the manufacturer and either body, and is non-binding, whereas meetings for scientific advice before Phase III trials have to date most often been tripartite (i.e., the manufacturer together with both). TGA and PBS have found the meetings useful, in terms of enhanced understanding and trust, although resource implications are an impediment, and manufacturers have to date provided limited feedback (5).

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Table 1. Overview of Interaction Initiatives

Region/ Country	Stakeholders	Type of interaction	Websites
Australia	TGA (Regulator) PBAC (Decision Maker)	Parallel submission/review	www.tga.gov.au www.health.gov.au
Australia	TGA (Regulator) PBS(Coverage body)	Scientific advice on development	www.tga.gov.au www.pbs.gov.au
Canada	Health Canada (Regulator) CADTH (HTA)	Parallel submission/review	www.hc-sc.gc.ca www.cadth.ca
England	MHRA (Regulator) NICE (Decision Maker)	Scientific advice on development	www.mhra.gov.uk www.nice.org.uk
Sweden	MPA (Regulator) TLV (Coverage body)	Scientific advice on development	www.lakemedelsverket.se www.tlv.se
USA	FDA (Regulator) CMS (Coverage body)	Parallel submission/review (devices)	www.fda.gov www.cms.gov
Europe	EMA (Regulator) EUnetHTA (HTA network)	Revision of EPARs	www.ema.europa.eu www.eunethta.net
Europe	EMA (Regulator) EUnetHTA (HTA network)	Harmonisation of HTA requirements	www.ema.europa.eu www.eunethta.net
Europe	Multiple stakeholders	Scientific advice on development (Tapestry)	www.tapestrynetworks.com
Europe	Multiple stakeholders	Orphan drug working party collaboration	ec.europa.eu/pharmaforum www.eucerd.eu/
Global	Multiple stakeholders	Scientific advice on development (Green Park Collaborative)	www.cmtpnet.org/gpc

Parallel Submissions (TGA and PBAC). Since January 2011, it is possible to submit an application for reimbursement to PBAC at any time after submission of the registration application to the TGA (1;5;19). However, because timelines for TGA typically are approximately 9 months, and those of PBAC around 4 months, certain constraints have been added to these parallel submissions: PBAC recommendations, publication or listing cannot be made public until after the TGA decision and consequent listing on the Australian Register of Therapeutic Goods.

Information sharing on devices (TGA and PDC). Information sharing has been improved regarding devices, because TGA now communicates its safety assessment outcomes with PDC, and vice-versa (5;19). As of 2011, PDC are automatically notified about new device applications to TGA. In addition, there is a possibility of parallel processing of co-dependent technologies, for example, a medical device in combination with a pharmaceutical.

Canada

Health Canada is responsible for evaluation of quality, safety and efficacy of drugs and medical devices in Canada. When a new drug achieves regulatory approval, Health Canada issues a Notice of Compliance (NOC) to the manufacturer. The Canadian Agency for Drugs and Technologies in Health (CADTH) is the national body that conducts HTA under the Common Drug Review (CDR), and provides a reimbursement recommendation to the publically funded drug plans in all provinces and territories in Canada (except Quebec), while price negotiation and budgetary impact considerations occur at the provincial level.

Parallel submissions (Health Canada and CADTH). In 2008, a regulatory-HTA collaboration pilot was initiated for priority drugs, defined as breakthrough drugs or drugs that could save at least $2.5 million to the CDR drug plans (5;19). For these drugs, manufacturers were allowed to send pre-NOC priority review submissions to CADTH, which screened submissions for eligibility (screening may include evaluation of the manufacturer's pharmacoeconomic analysis). Pilot submissions were filed within 60 to 90 days of anticipated NOC, but CADTH recommendations were not released until the NOC was issued.

The pre-NOC pilot was initiated through a joint retrospective analysis to identify areas for collaboration by using a case study approach (5;19). This resulted in methods of sharing information that were tested in a pilot of three drug submissions, and allowed access to the regulator's extensive knowledge in a therapeutic area together with the regulator's interpretation of information common with HTA. The pilot determined that information sharing between Health Canada and CADTH was beneficial, and resulted in an agreement that pre-NOC information sharing would continue beyond the pilot framework. Hence, since July 2009, manufacturers may request an HTA 90 days before license. There is now also a similar option to submit pre-NOC oncology drugs to the pan-Canadian Oncology Drug Review Process (pCODR).

Sweden

In Sweden, the Medical Products Agency (MPA) is responsible for regulation and surveillance of the development, manufacturing and marketing of pharmaceuticals. The Dental and Pharmaceutical Benefits Agency (TLV) is an independent government body responsible for determining whether a drug should be subsidized by the national Pharmaceutical Benefit Scheme.

Joint Scientific Advice (MPA and TLV). MPA offers the possibility for manufacturers to seek nonbinding advice on their drug development programs and submissions, whereas TLV do not provide such an option.

A pilot of joint MPA and TLV scientific advice meetings was run from September 2009 to June 2010 with the aim of contributing to a more rational and cost-effective use of pharmaceutical products (22). The purpose was also to meet enquiries from pharmaceutical industry as well as to improve interactions and understanding of methodologies between the two bodies. Advice was administered by MPA. In practice the applicant was asked to submit separate sets of questions to each of the bodies, which were discussed independently within each body. Then a short joint discussion was held immediately before the meeting with the applicant, where each body provided final responses to their respective questions.

After twelve joint advice meetings the pilot was evaluated and found to have met all of its objectives (5;19). From January 2011, MPA and TLV have agreed to provide joint advice on a regular basis, and are also considering providing the option of joint advice for postauthorization effectiveness studies.

United Kingdom

The Medicines and Healthcare products Regulatory Agency (MHRA) is responsible for evaluation of quality, safety and efficacy of pharmaceuticals and devices in the UK. The National Institute for Health and Clinical Excellence (NICE) is an independent organization responsible for appraising the clinical- and cost-effectiveness of pharmaceuticals and devices, and is currently the reimbursement decision maker for England and Wales.

Joint scientific advice in the UK (MHRA and NICE). Both MHRA and NICE provide the possibility for manufacturers to seek nonbinding advice on drug development programs and submissions. In March 2010, NICE and MHRA initiated a parallel scientific advice pilot to provide the option of simultaneous consultations with applicants. Although their advice is offered independently, all parties report increased awareness of important issues related a particular product (24).

United States

In the United States, the Food and Drug Administration (FDA) is responsible for evaluation of quality, safety and efficacy of pharmaceuticals and devices. Centers for Medicare and Medicaid Services (CMS) are responsible for assessing the clinical effectiveness of new medicines for reimbursement under the Medicare and Medicaid insurance programs.

Parallel review of medical devices pilot (FDA and CMS). In June 2010, the FDA and CMS issued a Memorandum of Understanding that allowed improved sharing of information between the agencies, and in September 2010, the FDA and CMS issued a proposal to initiate parallel review of medical devices for the purpose of reducing the time between FDA authorization and the CMS coverage decision (15). The pilot commenced in October 2011, and was available on a voluntary basis for up to five FDA-regulated medical devices per year (14).

TRANS-NATIONAL INTERACTIONS

Europe

Collaboration on EPAR content (EUnetHTA and EMA). The European Public Assessment Report (EPAR) is the scientific assessment report that EMA publishes after marketing authorization of a new medicine has been granted. EMA and the European network for HTA (EUnetHTA) have been collaborating since February 2010 to determine how the EPAR could improve its contents to aid EU Member State HTA organizations in their assessment of relative effectiveness (8). Comments and suggestions for improvements were provided by EUnetHTA and by the Medicine Evaluation Committee (MEDEV), an official committee of the European Social Health Insurance Forum (ESIP) (23). In 2010, the EPAR template was revised to be more informative for relative effectiveness assessments. EMA and EUnetHTA have an ongoing collaboration to evaluate the usefulness of the EPAR for health technology assessors.

Regulatory input into HTA methodology harmonization (EUnetHTA and EMA). Currently EUnetHTA is developing guidelines for relative effectiveness assessments (REA) of pharmaceuticals (9). These guidelines cover issues on how to compare different technologies, that is, which endpoints and quality assessment of the evidence should be used in an HTA. Under Work Package 5 of the EUnetHTA Joint Action, a pilot was conducted in partnership with the EMA and a manufacturer (10). The pilot assessed the usability of the guidelines for "rapid" REA, meaning assessment of a new medicine at the time of authorization. The pilot assessment and report development was conducted from May to November 2011, and involved 52 individuals from 24 HTA organizations. This was followed by a consultation phase from December 2011 to May 2012. The outcome of the pilot indicated that in general the EUnetHTA model for REA is feasible although further refinement was required (10).

Consultation in Early-stage Drug Development (Multi-stakeholder). In 2006, Tapestry Networks established the European Healthcare Innovation Leadership Network that included stakeholders from EU Member State healthcare bodies and industry. The purpose was to improve clarity and alignment among the stakeholders

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regarding value of a pharmaceutical and the evidence required to demonstrate that value most effectively (25).

In January 2010, the network initiated pilots of early multi-stakeholder consultations involving regulators, HTA and coverage bodies, patient representatives, clinicians, and pharmaceutical companies from France, Germany, Italy, the Netherlands, Sweden, the United Kingdom, and EMA (25). Three companies funded the network, and have each volunteered a product that was in development as a test case for the pilots. The pilots were conducted in October and December 2010, and February 2011, and the non-binding, non-written advice involved all participants regarding issues of therapeutic value. Additional advice involved a smaller group of HTA and coverage bodies regarding questions on economic value deriving from therapeutic benefits. A second phase of pilots commenced mid 2011.

European Orphan Drug Initiatives (Multi-stakeholder). In 2008, the EU High Level Pharmaceutical Forum recommended the creation of a Working Party collaboration on the scientific assessment of the Clinical Added Value of Orphan Drugs (CAVOD). The purpose was to provide common assessment reports to better inform national pricing and reimbursement decision making, and to reduce unequal patient access to medicines across Europe (12). In October 2011, the final CAVOD report was released which detailed plans for the creation of a mechanism to enable information flow about rare diseases and drugs to be shared amongst European stakeholders, with particular emphasis on developing a continuum between regulatory and HTA activities (13). This included a proposal for integration of the CAVOD process into EUnetHTA and the establishment of four pilots in 2012, one of which was to be an experiment on EUnetHTA and EMA interaction before market authorization (13).

GLOBAL

Green Park Collaborative (Multi-stakeholder). The Green Park Collaborative (GPC) is an initiative which has started as a pilot project to explore the scientific feasibility of developing international methodological guidance to industry on trial design and evidence generation to meet the needs of HTA organizations and coverage decision makers (16). Such guidance is intended to be informed by and aligned with related regulatory guidance where feasible and appropriate, and seeks to reduce the uncertainty faced by industry; to improve the relevance of the evidence generated through clinical research; and through this, to promote faster patient access to useful innovations. The pilot proceeds at the condition-specific level, by developing a guidance document which will provide recommendations on the design of clinical studies of pharmacologic therapies for Alzheimer's disease. The GPC is also considering a parallel pilot project to develop non–disease-specific methodological guidance on trial design and evidence generation (16).

Table 2. Organisations Promoting Broader International Dialogues

Acronym	Organisation/society/association	Website
CIRS	Centre for Innovation in Regulatory Science	www.cirsci.org
CMTP	Center for Medical Technology Policy	www.cmtpnet.org
DIA	Drug Information Association	www.diahome.org
HTAi	Health Technology Assessment International	www.htai.org
ISPOR	International Society for Pharmacoeconomics and Outcomes Research	www.ispor.org
TOPRA	The Organization for Professionals in Regulatory Affairs	www.topra.org

BROADER INTERNATIONAL DIALOGUE

Various organizations have arranged international meetings in recent years during which regulatory, HTA and coverage bodies, patient representatives and/or other stakeholders have had the opportunity to discuss the relationship between HTA and regulation and ways in which regulatory, HTA and coverage bodies can work together (Table 2).

DISCUSSION

Lessons Learned from Interaction Initiatives

It is evident from the proliferation of initiatives and international discussions in this area that many parties desire increased coordination of both processes and evidentiary requirements. Current initiatives and dialogues typically focus on processes of coordination of pre- and post-approval data requirements. These include how the information HTA and coverage bodies require on relative/comparative effectiveness best can be developed pre- and post-launch; what scope there is for improved coordination of requirements for regulatory approval and HTA, and for relative/comparative effectiveness information across coverage body jurisdictions; what role manufacturers, regulatory, HTA and coverage bodies have in defining and addressing these information requirements; how formal clinical guidance and decisions on reimbursement can be developed for unlicensed uses of a product within a healthcare system; and how data and data systems should be shared between stakeholders.

Scientific advice on the evidentiary requirements of HTA and coverage bodies (on trial design, modeling methodology, etc.) may enhance clarity for manufacturers, and joint advice involving HTA, coverage and regulatory bodies might promote better understanding of expectations among all stakeholders. However, the differing remits of each party involved do place limits upon the degree to which evidentiary expectations may be adjusted, and while early initiatives are promising, it remains to be demonstrated that these will ultimately facilitate more efficient reviews, enhanced predictability of evidentiary requirements for industry, and overall benefit for health systems.

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Table 3. Potential General Benefits and Challenges of Interaction Initiatives

Benefits	Challenges
For patients and clinicians: • Faster access to valuable products • Better understanding of the reasons for decisions made by regulators and HTA/coverage bodies, especially where these diverge *For industry:* • Faster market access • For international initiatives, opportunity to coordinate advice across multiple markets • Greater understanding about differences in evidence required by which bodies and when • Possibility of removing unnecessary barriers to successful development and appropriate market access for innovative products *For regulatory, HTA and coverage bodies:* • Improved coordination of evidentiary expectations among HTA, coverage and regulatory bodies • Increased alignment of methodological guidance and data requirements for establishing safety, efficacy, effectiveness, and comparative efficacy and effectiveness in so far as necessary and possible, and opportunity to clarify why requirements may be different • Better use of limited expertise and resources through reduction of review and advice duplication • Improved alignment of the timing and logistics of processes where appropriate *For all stakeholders:* • Increased opportunity for interaction between all stakeholders • Better awareness of the complementary roles of regulatory, HTA and coverage bodies • Increased transparency of approval and decision making processes • Opportunity for better use of limited expertise and resources • Opportunity to build trust and understanding	*For patients and clinicians:* • No, limited or too slow access to efficient products • Difficulties in understanding possible differences in decisions made by the different bodies *For industry:* • Concerns about the security of proprietary information if shared with HTA and coverage bodies • Satisfying evidentiary requirements from advices that may be difficult to achieve and/or resource demanding • Finding mechanisms to overcome possible conflicting advice • Concerns about the risk of increasing evidentiary burden *For regulatory, HTA and coverage bodies:* • Dealing with the differences in goals, priorities, relations with stakeholders, and ways of working between the different bodies • Concern that industry may not disclose all relevant information about a product • Legal constraints limiting information sharing between regulatory and other bodies • Limited feedback to agencies from industry after consultations reduces the ability to improve future advice • Stimulating industry in the uptake of post pilot joint-advice or parallel submission options • Dealing with possible lack of resources to continue initiatives beyond pilot phase *For all stakeholders:* • Dealing with jurisdictional and contextual differences such as differences in standard of care, economic and political priorities, and health care delivery context (particularly for international initiatives) • Insufficient understanding within regulatory, HTA, and coverage bodies and industry of respective purposes, remits, and processes • Finding best ways of involving clinicians and patients in discussions about the relationship between regulatory, HTA, and coverage processes • Establishing a standardised vocabulary to ensure common understanding • Challenges in establishing the legitimacy of international initiatives

Potential Benefits and Challenges of Interaction Initiatives

An overview of potential benefits and challenges based on the experience or views from the initiatives described above are presented in Table 3. Some benefits and challenges are common across stakeholder groups, whereas others vary among different stakeholders, in some cases according to whether initiatives are national or international. Initiatives with an international scope (e.g., Green Park Collaborative) may be of high value to industry because their outputs apply across multiple markets, and may reduce duplication of similar efforts in multiple jurisdictions. However, as compared with national initiatives, international initiatives face challenges in dealing with jurisdictional and contextual differences (e.g., differences in standard of care and relevant comparators, economic and political priorities, and healthcare delivery systems). International initiatives may face further challenges in establishing legitimacy for their outputs, because no single organization or body is empowered to act on behalf of HTA or coverage bodies globally.

The authors suggest that initiatives addressing the evidentiary expectations of HTA and regulatory bodies at the level of therapeutic areas, as opposed to the level of individual drugs, offer particular promise for maximizing the efficient use of scarce organizational resources and for generating outputs of wide relevance. Significant efficiencies for both the developer and the reviewing bodies may be realized if condition-specific as well as general methodological guidance is further advanced at the international level. The authors suggest that all initiatives in this field should adopt a long-term perspective that seeks to identify and address unmet health system needs.

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However, on the question of whether future initiatives concerning scientific advice and evidentiary expectations will be product-specific or condition-specific, national, or international, it is our belief that the answer is "yes to all the above". Detailed product-specific advice will always be needed, as will advice relevant to specific therapeutic areas.

Success Factors for HTA-Regulatory interactions

Among the initiatives described in this study, several common lessons may be drawn. The initiatives described have generally imposed significant resource demands upon participants, and this poses an inherent challenge for organizations operating under resource constraints. We therefore observe that critical success factors for HTA-regulatory interactions include institutional capacity, time and expertise, as well as effective processes, whether formal or informal, for prioritizing areas of collaboration (whether process-oriented, evidentiary, or other).

The initiatives described also frequently require organizations to work outside of their traditional remits, to engage with different stakeholders, and in some cases to adjust formal processes. Success in these areas requires a high degree of political support for the goals underpinning the initiatives, particularly when these may generate opposition among some groups. We further observe that because these initiatives require organizations to work across traditional boundaries and remits, they require a high degree of transparency and awareness of participants' respective responsibilities and constraints, both legal and organizational.

Moreover, it seems essential to (i) have a standardized lexicon to ensure common understanding, (ii) optimize the timing of interactions, and (iii) ensure separation of different steps in the process (i.e., regulatory, clinical added value, economic value, and decision making) to maximize the benefits and minimize the risks to all stakeholders. Finally, building on existing experiences and structures of interaction between stakeholders is likely to support the development of future interactions. These factors seem to hold across all types of interactions.

CONCLUSION

We consider that the present variety of initiatives will slowly coalesce as best practice is identified, and we foresee further clarification of roles and responsibilities as well as further alignment of methodological and technical requirements over the next 5 to 10 years. This study represents an attempt to reflect on current activities to inform future developments, and the authors believe that ongoing efforts to share lessons and experiences across jurisdictional lines will be critical to realizing the promise that current initiatives represent.

SUPPLEMENTARY MATERIAL

Supplementary Table 1: www.journals.cambridge.org/thc2012041

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CONFLICTS OF INTEREST

Logan Mardhani-Bayne's organization has received grants from several pharmaceutical companies and the World Health Organization to support scientific meetings. Chris Henshall receives a honorarium as Chair of the HTAi Policy Forum, consultancy fees from several public research organizations, and consultancy fees from several medical companies for chairing advisory boards. The other authors report no potential conflicts of interest.

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